

IN THE CLAIMS:

Please amend the claims to read as follows:

21 --24. (Amended) An *in vitro* method for identifying the repertoire of NKR inhibitory immunoreceptors within a subject wherein said immunoreceptors are selected from the group consisting of p58.1, p58.2, p70.INH, p140.NH, NKG2A and NKG2B receptors, these immunoreceptors being designated hereinafter target receptors, comprising:

- (i) contacting a nucleic acid sample derived from said subject with at least one pair of oligonucleotides, one being designated a 3' oligonucleotide and the other a 5' oligonucleotide, wherein the 3' and 5' oligonucleotides hybridize in a buffer comprising 20 mM Tris-HCl, pH 8.4; 50 mM KCl; 2.5 mM MgCl<sub>2</sub> at a temperature of between 50°C and 65°C, to a nucleic acid encoding a target receptor, but do not hybridize, under the same hybridization conditions, with a NKR activatory immunoreceptor counterpart and;
- (ii) detecting hybridization between the nucleic acid encoding the NKR inhibitory immunoreceptor and the 3' and 5' oligonucleotide pair(s),

wherein detection of hybridization between the nucleic acid encoding the NKR inhibitory immunoreceptor and the 3' and 5' oligonucleotide pair(s) identifies the repertoire of NKR inhibitory receptors.

25. (amended) An *in vitro* method for identifying the repertoire of NKR activatory immunoreceptors within a subject wherein said immunoreceptors are selected from the group consisting of p50.1, p50.2, p70.ACT, p140.ACT, NKG2C, NKG2D, NKG2E and NKG2F, these immunoreceptors being designated hereinafter target receptors, comprising:

- (i) contacting a nucleic acid sample derived from said subject with at least one pair of oligonucleotides, one being designated a 3' oligonucleotide and the other a 5' oligonucleotide, wherein the 3' and 5' oligonucleotides hybridize in a buffer comprising 20 mM Tris-HCl, pH 8.4; 50 mM KCl; 2.5 mM MgCl<sub>2</sub> at a temperature of between 50°C and 65°C, to a nucleic acid encoding a target receptor, but do not hybridize, under the same hybridization conditions, with a NKR inhibitory immunoreceptor counterpart: and;
- (ii) detecting hybridization between the nucleic acid encoding the NKR activatory immunoreceptor and the 3' and 5' oligonucleotide pair(s),

wherein detection of hybridization between the nucleic acid encoding the NKR activatory immunoreceptor and the 3' and 5' oligonucleotide pair(s) identifies the repertoire of NKR activatory receptors.

02 32. (amended) The method of claim 24 or 25 wherein the hybridization between the nucleic acid molecule encoding the NKR activatory or inhibitory immunoreceptors and the 3' and 5' oligonucleotide pairs is detected by resolution and visualization on a polyacrylamide gel of electrophoretic bands containing the said hybrids.

03 54. (Amended) The method of claim 24 or 25 wherein said method is used to predict or monitor the state of resistance of a subject to (i) infection, wherein said infection is viral, parasitic or bacterial (ii) autoimmune disease, or (iii) the development of malignant cells.

55. (Amended) The method of claim 24 or 25 wherein said method is used to screen for compositions which are used to reduce the symptoms associated with infectious autoimmune or proliferation disorders.

Please ~~cancel~~ claims 40-49, without prejudice.

Please ~~add~~ the following new claims:

04 --58. (New) An *in vitro* method for identifying the repertoire of NKR inhibitory immunoreceptors within a subject wherein said immunoreceptors are selected from the group consisting of p58.1, p58.2, p70.INH, p140.NH, NKG2A and NKG2B receptors, these immunoreceptors being designated hereinafter target receptors, comprising:

- (i) contacting a nucleic acid sample derived from said subject with at least one pair of oligonucleotides, one being designated a 3'

oligonucleotide and the other a 5' oligonucleotide, and wherein the 3' and 5' oligonucleotides hybridize in a buffer comprising 20 mM Tris-HCl, pH 8.4; 50 mM KCl; 2.5 mM MgCl<sub>2</sub> at a temperature of between 50°C and 65°C, to a nucleic acid encoding a target receptor, but do not hybridize, under the same hybridization conditions, with a NKR activatory immunoreceptor counterpart and wherein;

- (a) the 5' oligonucleotide comprises the sequence of SEQ ID No.1, and at least one 3' oligonucleotide selected from the group of 3' oligonucleotides comprising the sequence of SEQ ID No. 5, No. 2, No. 6 or No. 7; or
- (b) the 5' oligonucleotide comprises the sequence of SEQ ID No. 4 and at least one 3' oligonucleotide selected from the group of 3' oligonucleotide comprising the sequence of SEQ ID No. 5, No. 2, No. 6 or No. 7, or a sequence which is derived therefrom; or
- (c) the 5' oligonucleotide comprises the sequence of SEQ ID No. 9, or a sequence which is derived therefrom, and at least one 3' oligonucleotide selected from the group of 3' oligonucleotides comprising the sequence SEQ ID No. 5, No. 2, No. 6 or No. 7, or a sequence which is derived therefrom; or.

(d) at least one 5' oligonucleotide comprising the sequence of SEQ ID No. 10, No. 11, No. 12 or No. 13 is selected from the group consisting of a 3' oligonucleotide comprising the sequence SEQ ID No. 14, or a sequence which is derived therefrom; and

(ii) detecting hybridization between the nucleic acid encoding the NKR inhibitory immunoreceptor and the 3' and 5' oligonucleotide pair(s),

wherein detection of hybridization between the nucleic acid encoding the NKR inhibitory immunoreceptor and the 3' and 5' oligonucleotide pair(s) identifies the repertoire of NKR inhibitory receptors.

59. (New) An *in vitro* method for identifying the repertoire of NKR activatory immunoreceptors within a subject wherein said immunoreceptors are selected from the group consisting of p50.1, p50.2, p70.ACT, p140.ACT, NKG2C, NKG2D, NKG2E and NKG2F, these immunoreceptors being designated hereinafter target receptors, comprising:

(i) contacting a nucleic acid sample derived from said subject with at least one pair of oligonucleotides, one being designated a 3' oligonucleotide and the other a 5' oligonucleotide, wherein the 3' and 5' oligonucleotides

hybridize in a buffer comprising 20 mM Tris-HCl, pH 8.4;  
50 mM KCl; 2.5 mM MgCl<sub>2</sub> at a temperature of between  
50°C and 65°C, to a nucleic acid encoding a target receptor,  
but do not hybridize, under the same hybridization  
conditions, with a NKR inhibitory immunoreceptor  
counterpart and wherein;

- 04
- (a) the 3' oligonucleotide of a said 3' and 5' oligonucleotide pair, used for determining the repertoire of NKR activatory immunoreceptors, is capable, under the same said hybridization conditions, of hybridizing to a nucleic acid encoding KAR target receptor wherein said nucleic acid encodes the amino acid sequence Lys Ile Pro Phe Thr Ile (K I P F T I) or Lys Leu Pro Phe Thr Ile (K L P F T I) (SEQ ID No. 26 or 27); or
  - (b) the 5' oligonucleotide comprises the sequence of SEQ ID No. 1 and a 3' oligonucleotide comprising the sequence of SEQ ID No. 3; or
  - (c) the 5' oligonucleotide comprises the sequence of SEQ ID No. 8 and a 3' oligonucleotide comprising the sequence of SEQ ID No. 3; or

- (d) the 5' oligonucleotide comprising the sequence of SEQ ID No. 9 and a 3' oligonucleotide comprising the sequence SEQ ID No. 3; or
- (e) the 5' oligonucleotide comprises the sequence of SEQ ID No. 15 and a 3' oligonucleotide comprising the sequence SEQ ID No.13; and

- 04
- (ii) detecting hybridization between the nucleic acid encoding the NKR activatory immunoreceptor and the 3' and 5' oligonucleotide pair(s),

wherein detection of hybridization between the nucleic acid encoding the NKR activatory immunoreceptor and the 3' and 5' oligonucleotide pair(s) identifies the repertoire of NKR activatory receptors.

60. (New) An *in vitro* method for identifying the repertoire of NKR inhibitory immunoreceptors within a subject wherein said immunoreceptors are selected from the group consisting of p58.1, p58.2, p70.INH, p140.NH, NKG2A and NKG2B receptors, these immunoreceptors being designated hereinafter target receptors, comprising:

- (i) contacting a nucleic acid sample derived from said subject with at least one pair of oligonucleotides, one being designated a 3' oligonucleotide and the other a 5' oligonucleotide, and wherein the

3' and 5' oligonucleotides hybridize in a buffer comprising 20 mM Tris-HCl, pH 8.4; 50 mM KCl; 2.5 mM MgCl<sub>2</sub> at a temperature of between 50°C and 65°C, to a nucleic acid encoding a target receptor, but do not hybridize, under the same hybridization conditions, with a NKR activatory immunoreceptor counterpart and wherein said 3' and 5' oligonucleotide pairs are selected from the group consisting of:

- 04
- (a) a 5' oligonucleotide comprising the sequence of SEQ ID No. 16 and a 3' oligonucleotide comprising the sequence SEQ ID No. 17;
  - (b) a 5' oligonucleotide comprising the sequence of SEQ ID No. 18 and a 3' oligonucleotide comprising the sequence SEQ ID No. 17;
  - (c) a 5' oligonucleotide comprising the sequence of SEQ ID No. 19 and a 3' oligonucleotide comprising the sequence SEQ ID No. 17; and
  - (d) a 5' oligonucleotide comprising the sequence of SEQ ID No. 20 and a 3' oligonucleotide comprising the sequence SEQ ID No. 21; and
- (ii) detecting hybridization between the nucleic acid encoding the NKR inhibitory immunoreceptor and the 3' and 5' oligonucleotide pair(s),



wherein detection of hybridization between the nucleic acid encoding the NKR inhibitory immunoreceptor and the 3' and 5' oligonucleotide pair(s) identifies the repertoire of NKR inhibitory receptors.

61. (amended) An *in vitro* method for identifying the repertoire of NKR activatory immunoreceptors within a subject wherein said immunoreceptors are selected from the group consisting of p50.1, p50.2, p70.ACT, p140.ACT, NKG2C, NKG2D, NKG2E and NKG2F, these immunoreceptors being designated hereinafter target receptors, comprising:

- (i) contacting a nucleic acid sample derived from said subject with at least one pair of oligonucleotides, one being designated a 3' oligonucleotide and the other a 5' oligonucleotide, wherein the 3' and 5' oligonucleotides hybridize in a buffer comprising 20 mM Tris-HCl, pH 8.4; 50 mM KCl; 2.5 mM MgCl<sub>2</sub> at a temperature of between 50°C and 65°C, to a nucleic acid encoding a target receptor, but do not hybridize, under the same hybridization conditions, with a NKR inhibitory immunoreceptor counterpart and wherein said 3' and 5' oligonucleotide pairs are selected from the group consisting of:

- 04
- (a) a 5' oligonucleotide comprising the sequence of SEQ ID No. 16 and a 3' oligonucleotide comprising the sequence SEQ ID No. 17;
  - (b) a 5' oligonucleotide comprising the sequence of SEQ ID No. 18 and a 3' oligonucleotide comprising the sequence SEQ ID No. 17;
  - (c) a 5' oligonucleotide comprising the sequence of SEQ ID No. 19 and a 3' oligonucleotide comprising the sequence SEQ ID No. 17; and
  - (d) a 5' oligonucleotide comprising the sequence of SEQ ID No. 20 and a 3' oligonucleotide comprising the sequence SEQ ID No. 21; and

- (ii) detecting hybridization between the nucleic acid encoding the NKR activatory immunoreceptor and the 3' and 5' oligonucleotide pair(s),

wherein detection of hybridization between the nucleic acid encoding the NKR activatory immunoreceptor and the 3' and 5' oligonucleotide pair(s) identifies the repertoire of NKR activatory receptors.

62. (New) The method of claim 58, 59, 60 or 61 wherein said method is used to predict or to monitor the acceptance or rejection, by a subject, of cells, tissue or organ which are genetically different.

63. (New) The method according to claim 58, 59, 60 or 61 wherein said method is used to predict or to monitor the safety or the pathogenicity (GVH), for a subject, of a graft or transplant, of cells, tissue or organ which are genetically different.

64. (New) The method according to claim 58, 59, 60 or 61 wherein said method is used to predict or to monitor for a subject of a GVL-type effect on the part of cells, tissue or organ which are genetically different.

65. (New) The method of claim 58, 59, 60 or 61 wherein said method is used to determine the state of activation of NK and/or T cells within a subject.

66. (New) The method of claim 58, 59, 60 or 61 wherein said method is used to predict or monitor the state of resistance of a subject to (i) infection, wherein said infection is viral, parasitic or bacterial (ii) autoimmune disease, or (iii) the development of malignant cells.

67. (New) The method of claim 58, 59, 60 or 61 wherein said method is used to screen for compositions which are used to reduce the symptoms associated with infectious autoimmune or proliferation disorders.

68. (New) A kit for carrying out the method of claim 58, 59, 60 or 61 comprising a container, at least one said 3' and 5' oligonucleotide pair, and reagents for carrying out the said method.

69. (New) The kit of claim 68 wherein said 3' and 5' oligonucleotide pair is coupled to a marker.

70. (New) The method of claim 58, 59, 60 or 61 wherein the 3' or 5' oligonucleotides are coupled to a marker, allowing detection of hybridization between the nucleic acid sample and the 3' and 5' oligonucleotides.

71. (New) The method of claim 70 wherein the marker is a fluorescence marker.

72. (New) The method of claim 70 wherein the marker is a radioactive marker.

73. (New) The method of claim 58, 59, 60 or 61 wherein the 3' and 5' oligonucleotide pair(s) serve(s) as 3' and 5' primers, respectively, for extension by DNA polymerase.

74. (New) The method of claim 58, 59, 60 or 61 wherein hybridization between the nucleic acid sample and the 3' and 5' oligonucleotide pair is detected by PCR amplification.

75. (New) The method of claim 58, 59, 60 or 61 wherein amplification is by nested PCR.

76. (New) The method of claim 58, 59, 60 or 61 wherein the hybridization between the nucleic acid molecule encoding the NKR activatory or inhibitory immunoreceptors and the 3' and 5' oligonucleotide pairs is detected by resolution and visualization on a polyacrylamide gel and visualization of electrophoretic bands containing the said hybrids.

77. (New) The method of claim 58 wherein said method is used to document the genotypic repertoire of KIR immunoreceptors.

78. (New) The method of claim 58 wherein said method is used to document the expression repertoire of KIR immunoreceptors.

79. (new) The method of claim 59 wherein said method is used to document the genotypic repertoire of KAR immunoreceptors.

80. (New) The method of claim 59 wherein said method is used to document the expression repertoire of KAR immunoreceptors.

81. (New) The method of claim 58, 59, 60 or 61 wherein the nucleic acid sample is of human or animal origin.

82. (New) The method of claim 58, 59, 60 or 61 wherein the nucleic acid sample is derived from blood, bone marrow, lymphocytes, NK and/or T cells or transgenic cells.

83. (New) The method of claim 58, 59, 60 or 61 wherein the nucleic acid sample is a genomic or cDNA library.--

#### R E M A R K S

Claims 24-57 are currently pending. Claims 24-55 are rejected under 35 U.S.C. § 112, second paragraph. Claims 24-26, 28, 30 and 32-39 are rejected under 35 U.S.C. §102(b). Claims 24-39 and 50-55 are rejected under 35 §103. The Examiner has